

PATENT 98/05127
BUNDESREPUBLIK DEUTSCHLAND

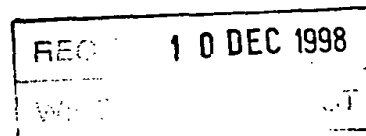
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EPO-DG 1

02. 12. 1998

Bescheinigung



Die Firma Memorec Stoffel GmbH in Köln/Deutschland hat eine Patentanmeldung unter der Bezeichnung

"Neutrale Sphingomyelinase der Maus und des Menschen und diese überxprimierende Säuger- und Nicht-Säugerkzellen"

als Zusatz zur Patentanmeldung 197 34 764.9

am 15. Oktober 1997 beim Deutschen Patentamt eingereicht.

Das angeheftete Stück ist eine richtige und genaue Wiedergabe der ursprünglichen Unterlage dieser Patentanmeldung.

Die Anmeldung hat im Deutschen Patentamt vorläufig die Symbole C 12 N, C 12 Q und G 01 N der Internationalen Patentklassifikation erhalten.

München, den 22. Oktober 1998

Der Präsident des Deutschen Patentamts

Im Auftrag

Agurks

Aktenzeich n: 197 58 501.9

murine nSMase

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1  GTGCTGGTGG AAGCCGAGCC GGAACAAGG GAGGAACCTG TAGGMC GCGG
51  TGCGGAGAAC CCACCGAAGG ACCTAAGAAT CTGGAACAGT CCACCCGAGA
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201 GTAGCCCCCC ACCCCAACC AGCTCGCGTT CCTGGGTCGG GGCAGCGCAG
251 GACAGGGCAA TAAGCCTGTG CGCGCAATCC GCCTCGCCGC CCTTGCTCCG
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351 ATCTCAACTG CTGGGACATC CCCTACCTGA GCAAACATAG GGCGGACCGC
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451 CCTGGAGGAG GTGTGGAGTG AGCAGGACTT CCAGTACCTA AGGCAAAGGC
501 TATCGCTCAC CTATCCAGAT GCACACTACT TCAGAAGCGG GATGATAGGC
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601 TGTCTACAGT CTGAATGGTT ACCCTACAT GTTCCATCAT GGAGACTGGT
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1301 GTGATCGTTT GGGGGCTGTC CCTTCTGGTG TTGCTGTGTG TCCTGGCTGC
1351 AGGAGAAGAG GCCAGGGAAG TGGCCATCAT CCTCTGCATA CCCAGTGTGG
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1601 CACAAAAAAA AAAAAAAAAA AAAAAAAAAA AAA

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human nSMase

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151 CTGATTGGGA ACAGCCGGCC GGTGCGCGG GGAACGCGGG AGTCGGGCCC
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251 AAGGAACGGT CTAGGGAGAA GGCGCCGCG GCGCCCCCG TCCCCACCGC
301 GGCCGTCGCT GGAGAGTTCG AGCGCCTAG CGCCCTGGA GCTCCCCAAC
351 CATGAAGCTC AACTTCTCCC TGCGACTGCG GATCTTCAAC CTCAACTGCT
401 GGGGCATPCC GTACTTGAGC AAGCACCGGG CCGACCGCAT GAGGCGCCTG
451 GGAGACTTTC TGAACCAGGA GAGCTTCGAC CTGGCTTTGC TGGAGGAGGT
501 TGGGAGTGAG CAGGACTTCC AGTACCTGAG ACAGAAGCTG TCACCTACCT
551 ACCCAGCTGC ACACCACTTC CGGAGCGGAA TCATTGGCAG TGGCCTCTGT
601 GTCTTCTCCA AACATCCAAT CCAGGAGCTT ACCCAGCACA TCTACACTCT
651 CAATGGCTAC CCCTACATGA TCCATCAAtg tgactggttc agTGGGAAGG
701 CTGTGGGGCT GCTGGTGCTC CATCTAAGTG GCATGGTGCT CAACGCCTAT
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1651 AAAA

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20
1

mouse nSMase transl. [313 to 1572] -> 1-phase Translation

DNA sequence 1632 b.p. GTGCTGGTGGAA ... AAAAAAAAAA linear

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met lys leu asn phe ser leu arg leu arg	val phe asn leu asn cys trp asp ile pro	403 / 31	TAC CTG AGC AAA CAT AGG GCG GAC CGC ATG AAG CGC TTG GGA GAC TTT CTG AAC TTG GAA
373 / 21	tyr leu ser lys his arg ala asp arg met lys arg leu gly asp phe leu asn leu glu	463 / 51	AAC TTT GAT CTG GCT CTC CTG GAG GAG GTG TGG AGT GAG CAG GAC TTC CAG TAC CTA AGG
433 / 41	asn phe asp leu ala leu leu glu glu val trp ser glu gln asp phe gln tyr leu arg	523 / 71	493 / 61
CAA AGG CTA TCG CTC ACC TAT CCA GAT GCA CAC TAC TTC AGA AGC GGG ATG ATA GGC AGT	gln arg leu ser leu thr tyr pro asp ala his tyr phe arg ser gly met ile gly ser	583 / 91	553 / 81
GGC CTC TGT GTG TTC TCC AAA CAC CCA ATC CAG GAA ATC TTC CAG CAT GTC TAC AGT CTG	gly leu cys val phe ser lys his pro ile gln glu ile phe gln his val tyr ser leu	643 / 111	613 / 101
AAT GGT TAC CCC TAC ATG TTC CAT CAT GGA GAC TGG TTC TGT GGG AAG TCT GTG GGG CTG	asn gly tyr pro tyr met phe his his gly asp trp phe cys gly lys ser val gly leu	703 / 131	673 / 121
CTG GTG CTC CGT CTA AGT GGA CTG GTG CTC AAT GCC TAC GTG ACT CAT CTA CAT GCT GAG	leu arg leu ser gly leu val leu asn ala tyr val thr his leu his ala glu	763 / 151	733 / 141
CGA CAG AAG GAC ATC TAC TTT GCA CAC CGT GTG GGC CAA GCT TGG GAA CTG GCC	tyr ser arg gln lys asp ile tyr phe ala his arg val ala gln ala trp glu leu ala	823 / 171	793 / 161
CAG TTC ATC CAC CAC ACA TCC AAG AAT GCA GAT GTG GTT CTA TTG TGT GGA GAC CTC AAT	gln phe ile his his thr ser lys asn ala asp val val leu leu cys gly asp leu asn	883 / 191	853 / 181
ATG CAC CCC AAA GAC CTG GGC TGC TGC CTG CTG AAA GAG TGG ACA GGG CTC CAT GAT GCT	met his pro lys asp leu gly cys cys leu leu lys glu trp thr gly leu his asp ala	943 / 211	913 / 201
TTC GTT GAG ACT GAG GAC TTT AAG GGC TCT GAT GAT GGC TGT ACC ATG GTA CCC AAG AAC	phe val glu thr glu asp phe lys gly ser asp asp gly cys thr met val pro lys asn	1003 / 231	973 / 221
TGC TAC GTC AGC CAG CAG GAC CTG GGA CCG TTT CCG TCT GGT ATC CGG ATT GAT TAC GTG	cys tyr val ser gln gln asp leu gly pro phe pro ser gly ile arg ile asp tyr val	1063 / 251	1033 / 241
CTT TAC AAG GCA GTC TCT GAG TTC CAC GTC TGC TGT GAG ACT CTG AAA ACC ACT ACA GGC	leu tyr lys ala val ser glu phe his val cys cys glu thr leu lys thr thr thr gly	1123 / 271	1093 / 261
TGT GAC CCT CAC AGT GAC AAG CCC TTC TCT GAT CAC GAG GCC CTC ATG GCT ACT TTG TAT	cys asp pro his ser asp lys pro phe ser asp his glu ala leu met ala thr leu tyr	1183 / 291	1153 / 281
CAC AGC CCC CCT CAG GAA GAC CCC TGT ACT GCC TGT GGC CCA CTG GAA AGG TCC	his ser pro pro gln glu asp pro cys thr ala cys gly pro leu glu arg ser	1243 / 311	1213 / 301
GAT TTG ATC AGC GTG CTA AGG GAG GCC AGG ACA GAG CTG GGG CTA GGC ATA GCT AAA GCT	asp leu ile ser val leu arg glu ala arg thr glu leu gly leu gly ile ala lys ala	1303 / 331	1273 / 321
CGC TGG TGG GCT GCA TTC TCT GGC TAT GTG ATC GTT TGG GGG CTG TCC CTT CTG GTG TTG	arg trp trp ala ala phe ser gly tyr val ile val trp gly leu ser leu leu val leu	1363 / 351	1333 / 341
CTG TGT GTC CTG GCT GCA GGA GAA GAG GCC AGG GAA GTG GCC ATC ATC CTC TGC ATA CCC	leu cys val leu ala ala gly glu glu ala arg glu val ala ile ile leu cys ile pro	1423 / 371	1393 / 361
AGT GTG GGT CTG GTG CTG GTA GCA GGT GCA GTC TAC CTC TTC CAC AAG CAG GAG GCC AAG	ser val gly leu val leu val ala gly ala val tyr leu phe his lys gln glu ala lys	1483 / 391	1453 / 381
GGC TTA TGT CGG GCC CAG GCT GAG ATG CTG CAC GTT CTG ACA AGG GAA ACG GAG ACC CAG	gly leu cys arg ala gln ala glu met leu his val leu thr arg glu thr glu thr gln	1543 / 411	1513 / 401
GAC CGA GGC TCA GAG CCT CAC CTA GCC TAC TGC TTG CAG CAG GAG GGG GAC AGA GCT TAA	asp arg gly ser glu pro his leu ala tyr cys leu gln gln glu gly asp arg ala OCH		

28

human nSMase transl. [352 to 1623] -> 1-phase Translation

DNA sequence 1654 b.p. GACCGCCGGGGA ... AAAAAAAAAA linear

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met lys leu asn phe ser leu arg leu arg ile phe asn leu asn cys trp gly ile pro
412 / 21 442 / 31
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tyr leu ser lys his arg ala asp arg met arg arg leu gly asp phe leu asn gln glu
472 / 41 502 / 51
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ser phe asp leu ala leu leu glu glu val trp ser glu gln asp phe gln tyr leu arg
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CAG AAG CTG TCA CCT ACC TAC CCA GCT GCA CAC CAC TTC CGG AGC GGA ATC ATT GGC AGT
gln lys leu ser pro thr tyr pro ala ala his his phe arg ser gly ile ile gly ser
592 / 81 622 / 91
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gly leu cys val phe ser lys his pro ile gln glu leu thr gln his ile tyr thr leu
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asn gly tyr pro tyr met ile his his gly asp trp phe ser gly lys ala val gly leu
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tyr asn arg gln lys asp ile tyr leu ala his arg val ala gln ala trp glu leu ala
832 / 161 862 / 171
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952 / 201 982 / 211
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tyr leu glu thr arg asp phe lys gly ser glu glu gly asn thr met val pro lys asn
1012 / 221 1042 / 231
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1072 / 241 1102 / 251
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TTT GAC CCT CAC AGT GGC ACC CCC CTC TCT GAT CAT GAA GCC CTG ATG GCT ACT CTG TTT
phe asp pro his ser gly thr pro leu ser asp his glu ala leu met ala thr leu phe
1192 / 281 1222 / 291
GAC AGC CCC CCA CAG CAG AAC CCC AGC TCT ACC CAC GGA CCA GCA GAG AGG TCG
his ser pro pro gln gln asn pro ser ser thr his gly pro ala glu arg ser
1252 / 301 1282 / 311
CCG TTG ATG TGT GTG CTA AAG GAG GCC TGG ACG GAG CTG GGT CTG GGC ATG GCT CAG GCT
pro leu met cys val leu lys glu ala trp thr glu leu gly leu gly met ala gln ala
1312 / 321 1342 / 331
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arg trp trp ala thr phe ala ser tyr val ile gly leu gly leu leu leu ala leu
1372 / 341 1402 / 351
CTG TGT GTC CTG GCG GCT GGA GGA GGG GCC GGG GAA GCT GCC ATA CTG CTC TGG ACC CCC
leu cys val leu ala ala gly gly gly ala gly glu ala ala ile leu leu trp thr pro
1432 / 361 1462 / 371
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ser val gly leu val leu trp ala gly ala phe tyr leu phe his val gln glu val asn
1492 / 381 1522 / 391
GGC TTA TAT AGG GCC CAG GCT GAG CTC CAG CAT GTG CTA GGA AGG GCA AGG GAG GCC CAG
gly leu tyr arg ala gln ala glu leu gln his val leu gly arg ala arg glu ala gln
1552 / 401 1582 / 411
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1612 / 421
AAA GAA CAA TAA
lys glu gln OCH

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49

70135

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 851 CCAAGAAGGC AGACGTGGTT CTGTTGTGTG GAGACCTCAA CATGCACCCA
 901 GAAGACCTGG GCTGCTGCCT GCTGAAGGAG TGGACAGGGC TTCATGATGC
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 1151 CCCCCCTCTC TGATCATGAA GCCCTGATGG CTACTCTGTT TGTGAGGCAC
 1201 AGCCCCCACC AGCAGAACCC CAGCTCTACC CACGGACCAG CAGAGAGGTC
 1251 GCCGTTGATG TGTGTGCTAA AGGAGGCCTG GACGGAGCTG GGTCTGGGCA
 1301 TGGCTCAGGC TCGCTGGTGG GCCACCTTCG CTAGCTATGT GATTGGCCTG
 1351 GGGCTGCTTC TCCTGGCACT GCTGTGTGTC CTGGCGGCTG GAGGAGGGGC
 1401 CGGGGAAGCT GCCATACTGC TCTGGACCCC CAGTGTAGGG CTGGTGCTGT
 1451 GGGCAGGTGC ATTCTACCTC TTCCACGTAC AGGAGGTCAA TGGCTTATAT
 1501 AGGGCCCAGG CTGAGCTCCA GCATGTGCTA GGAAGGGCAA GGGAGGCCCA
 1551 GGATCTGGGC CCAGAGCCTC AGCCAGCCCT ACTCCTGGGG CAGCAGGAGG
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 1651 AAAA

underlined is the coding sequence

mouse nSMase

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 51 TCGGAGAAAC CCACCGAAGG ACCTAAGAAT CTGGAACAGT CCACCCGAGA
 101 TTCCTTCCAG GACTGCCGGC GGCCTCGCGC AGCCAGCCCG GGATTTCAG
 151 CCGACCTTCT TTCCGGGTGG AAGGACGGCC TTGTGCCAG TAACGCAGGA
 201 GTAGCCCCC ACCCCCAACC AGCTCGCGTT CCTGGGTCGG GGCAGCGCAG
 251 GACAGGGCAA TAAGCCTGTG CGCGCAATCC GCCTCGCCGC CCTTGCTCCG
 301 AAGCACTCCA GCCATGAAGC TCAACTTTTC TCTACGGCTG AGAGTTTCA
 351 ATCTCAACTG CTGGGACATC CCCTACCTGA GCAAACATAG GCGGACCGC
 401 ATGAAGCGCT TGGGAGACTT TCTGAACTTG GAAAACCTTG ATCTGGCTCT
 451 CCTGGAGGAG GTGTGGAGTG AGCAGGACTT CCAGTACCTA AGGCAAAGGC
 501 TATCGCTCAC CTATCCAGAT GCACACTACT TCAGAAGCGG GATGATAGGC
 551 AGTGGCCTCT GTGTGTTCTC CAAACACCCA ATCCAGGAAA TCTTCCAGCA
 601 TGTCTACAGT CTGAATGGTT ACCCCTACAT GTTCCATCAT GGAGACTGGT
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 701 CTCAATGCCT ACGTGACTCA TCTACATGCT GAGTACAGCC GACAGAAGGA
 751 CATCTACTTT GCACACCGTG TGGCCCAAGC TTGGGAACTG GCCCAGTTCA
 801 TCCACCACAC ATCCAAGAAT GCAGATGTGG TTCTATTGTG TGGAGACCTC
 851 AATATGCACC CCAAAGACCT GGGCTGCTGC CTGCTGAAAG AGTGGACAGG
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 1001 CCGTTTCCGT CTGGTATCCG GATTGATTAC GTGCTTTACA AGGCAGTCTC
 1051 TGAGTTCCAC GTCTGCTGTG AGACTCTGAA AACCCTACA GGCTGTGACC
 1101 CTCACAGTGA CAAGCCCTTC TCTGATCAG AGGCCCTCAT GGCTACTTTG
 1151 TATGTGAAGC ACAGCCCCC TCAGGAAGAC CCCTGTACTG CCTGTGGCCC
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 1301 GTGATCGTTT GGGGGCTGTC CTTTCTGGTG TTGCTGTGTG TCCTGGCTGC
 1351 AGGAGAAGAG GCCAGGGAAG TGGCCATCAT CCTCTGCATA CCCAGTGTGG
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 1451 AAGGGCTTAT GTCGGGCCCA GGCTGAGATG CTGCACGTTT TGACAAGGGA
 1501 AACGGAGACC CAGGACCGAG GCTCAGAGCC TCACCTAGCC TACTGCTTGC
 1551 AGCAGGAGGG GGACAGAGCT TAAGAGCTTA ACAATAAAAC TTGCTTGACA
 1601 CACAAAAAAA AAAAAAAAAA AAAAAAAAAA AAA

human nSMase

1 GACCGCCGGG GACGAGCTTG GAGGAAAAGG AACCAGGAGC CGCCACCCG
 51 GGGGCGCTCT CCGGACCCCG AGGGTCCTAG CGCGCGGCC TTACCGAGCC
 101 TGGGCGCCCG GATTTCGGGA GCGGATCGCC TTTCCGGGTT GCGGCCCCG
 151 CTGATTGGGA ACAGCCGGCC GGTTCGCGGG GGAACGCGGG AGTCGGGCCC
 201 GACCTGAGCC ACGCGGGCTT GTTGCCACC TGTGCGCGCC GCCTGCGAAG
 251 AAGGAACGGT CTAGGGAGAA GCGCGCGCC GCGCCCCCG TCCCCACCG
 301 GGCCGTCGCT GGAGAGTTCG AGCCGCTAG CGCCCTGGA GCTCCCCAAC
 351 CATGAAGCTC AACTTCTCCC TGCGACTGCG GATCTTCAAC CTCAACTGCT
 401 GGGGCATTCG GTACTTGAGC AAGCACCAGG CCGACCGCAT GAGCGCCTG
 451 GGAGACTTTC TGAACCAGGA GAGCTTCGAC CTGGCTTTGC TGGAGGAGGT
 501 GTGGAGTGAG CAGGACTTCC AGTACCTGAG ACAGAAGCTG TCACCTACCT
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 601 GTCTTCTCCA AACATCCAAT CCAGGAGCTT ACCCAGCACA TCTACACTCT
 651 CAATGGCTAC CCCTACATGA TCCATCAtaa taactaatlc adTGGGAAGG
 701 CTGTGGGGCT GCTGGTGCTC CATCTAAGTG GCATGGTGCT CAACGCCTAT
 751 GTGACCCATC TCCATGCCGA ATACAATCGA CAGAAGGACA TCTACCTAGC

